PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RLL-266WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/02186	International filing date *(day/month/year)* 09.06.2003	Priority date *(day/month/year)* 07.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/24, A61K9/24		
Applicant RANBAXY LABORATORIES LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07.01.2004	14.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Sindel, U Telephone No. +49 89 2399-7064

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/02186

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-38 as originally filed

Claims, Numbers

1-117 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 19-25, 40-67, 71, 73-77, 104-107, 110-117

   because:

   ☒ the said international application, or the said claims Nos. 73-77 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 19-25, 40-67, 71, 74-75, 104-107, 110-117 are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. see search report .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	10-11, 18, 26-28, 36, 72, 101-103, 108-109
	No:	Claims	1-9, 12-14, 29-35, 37-39, 68-70, 73, 76-77
Inventive step (IS)	Yes:	Claims	
	No:	Claims	10-11, 18, 26-28, 36, 72, 101-103, 108-109
Industrial applicability (IA)	Yes:	Claims	1-14, 18, 26-39, 68-70, 72, 101-103, 108-109
	No:	Claims	

2. Citations and explanations

   see separate sheet

Reference is made to the documents cited in the search report. They are numbered accordingly. The document D5 was not cited in the international search report. A copy of the document is appended hereto.

D5: Hunnius - Pharmazeutisches Wörterbuch. Walter de Gruyter Verlag, Berlin, 7th ed., 1993, page 1497

Item III

1) Claims 73-77 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

2) Claims 19-25, 41-67, 71, 74-75, 104-107 and 110-117 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The term "waxy material" used in these claims is unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).
Furthermore, in claims 19, 43 and in the description on page 6, lines 13-19, it is defined that the "waxy material may be one or more polyethylene glycols (PEG) of one or more molecular weights". This definition is incorrect since the technical term "wax" stands for mixtures of various esters of straight-chain fatty acids (C_{18}-C_{34}) esterified with straight-chain monohydric alcohols (see D5). Hence, polyethylene glycol is not a wax.
The subject-matter of claim 40 is not clear since the terms "metformin XL" and "glipizide XL" are not closer defined and it is also not obvious if the choice of pharmaceutical ingredients shall be taken of the pairs of actives mentioned or if also single actives from this list can be comprised in the multiple unit dosage form.

Item IV

The Examining Division agrees with the objection put forward by the International Searching Authority as to lack of unity (Rule 13 PCT). The separate groups of inventions are:

1. Claims 1-14, 18-40, 41-67 (part.), 68-72, 73-77 (part.),101-103, 108-109, 114-117

Multiple unit dosage form, each unit comprising at least one core, a first coating layer and an outer layer

2. Claims 15-17, 41-67 (part.), 73-77 (part.), 104-107,110-113
Multiple unit dosage form, each unit comprising at least one core, a first coating layer, one or more additional layers and an outer layer

3. Claims 78-81, 85-100
Multiple unit dosage form, each unit comprising at least one core and a coating layer

4. Claims 82-84
Combination drug comprising two different multiple unit dosage forms

Multiple unit dosage forms having a different structure, in so far as the number of coating layers is different, as well as a combination drug comprising two different multiple unit dosage forms, show a priori a lack of unity.

Item V

The opinion expressed as to novelty, inventive step and industrial applicability refers only to matter for which an international search report has been drawn up (Rule 66.1(e) PCT).

1) Novelty

The subject matter of claims 1-9, 12-14, 29-35, 37-39, 68-70, 73 and 76-77 is not regarded as new in the sense of Article 33(2) PCT.
The prior art describes already coated multiple unit dosage forms with the following technical features:

D1: Modified release multiple unit dosage form with a lornoxicam pellet core, inner and outer coating layer. Core: Tween 20, cellulose, lactose, carboxymethylcellulose. Inner coating: hypromellose, Eudragit and Mg-stearat. Outer coating: hypromellose. The multiple unit dosage form can be compressed in tablets or filled in capsules (see example 1, claim 51 and page 33, lines 31-35).

D2: Modified release multiple unit dosage form with potassium chloride core, inner and outer coating layer. Core: potassium chloride and Na-carboxymethylcellulose. Inner coating: methocel, Eudragit and talc. Outer coating: methocel, talc. The

multiple unit dosage form can be compressed in tablets (see examples 2, 7 and abstract).

D3: Modified release multiple unit dosage form with inert core, first and outer coating layer. Core: sand, sugar, plastic. First coating: furosemid and PVP. Outer coating: HPMC, ethylcellulose, triethyl citrate (see claim 1, examples 1 and 5).

Hence, the subject-matter of present claims 1-9, 12-14, 29-35, 37-39, 68-70, 73 and 76-77 is not new.

The applicant is informed that there exists an intermediate document (D4) which might become relevant in the European Phase of the application.

2) **Inventive step**

The subject matter of claims 10-11, 18, 26-28, 36, 72, 101-103 and 108-109 does not involve an inventive step in the sense of Article 33(3) PCT.
The problem to be solved with the present application is the provision of multiple unit dosage forms with enough mechanical strength to stand the mechanical stress due to compression or filling.
The solution presented is a multiple unit dosage form with polyethylene glycol as outermost coating.
The Applicant shows the mechanical strength of the multiple unit dosage forms of the present application by comparing the release profile of the multiple units with the one of a tablet compressed of these units (see example 1). Nevertheless, there is no data provided showing the superior qualities of the multiple unit dosage forms of the present application compared to the ones of the prior art. In order to enable the Examining Division to appreciate the presence of an inventive step, the Applicant is kindly requested to submit data showing that the problem has really been solved and that the present dosage form has superior properties when compared to the prior art.

3) **Industrial applicability**

For the assessment of the present claims 73-77 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however,

claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment. The subject matter of present claims 1-14, 18, 26-39, 68-70, 72, 101-103 and 108-109 is industrially applicable.